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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,043	CANTOR ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-18 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-18 is/are rejected.

7)☒ Claim(s) 17 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 13 July 2005 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 7/31/2006 ; 10/10/2006.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 are pending and examined on the merits.

Information Disclosure Statement

The references of the IDS submitted on 7/31/2006 have been considered. The IDS of 10/10/2006 has been considered, however it is noted that the references cited in the IDS of 10/10/2006 are not initialed and are lined through because all of the references cited on the IDS of 10/10/2006 are duplicates of the references cited on the IDS of 7/31/2006.

Specification

1. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See for example p.7 ¶[021], p.13 ¶[051] and ¶[052]. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

2. Claim 17 is objected to because of the following informalities:

Step (e) of claim 17 recites the phrase 'at least one polymorphic markers', in which there is not agreement between the singular 'one polymorphic' and the plural 'markers'.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-11, 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11 are unclear over the recitation of the phrase 'the diluted single nucleotide dilution', as recited in each of independent claims 1 and 9 (each step (b)) because there is no antecedent basis in the claims for a single nucleotide dilution. Additionally, it is unclear how a haplotype, which comprises several polymorphic positions, can be detected in a target that is diluted to a single nucleotide.

Claims 1-11 are unclear over the recitation of the phrase 'the nucleic acid template' as recited in step (b) of claim 1, because there is not proper antecedent basis for any 'nucleic acid template' in the claims.

Claims 4-6 are unclear over the recitation of the phrase 'the polymorphism', as recited in each of claims 4-6. Claim 1, from which the rejected claims depend, recites only the plural 'polymorphic sites', thus it is unclear as to which of the multiple polymorphic markers is 'the polymorphism'.

Claims 17 and 18 are unclear over recitation of the phrase 'amplifying the diluted and undiluted nucleic acid sample', as recited in step (c) of claim 17. The phrase is unclear because claim 17 requires digesting a nucleic acid sample and diluting the

digested sample (steps (a) and (b) of claim 17), thus the claims do not provide for any undiluted sample after step (b).

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 2, and 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Ruano et al (1990) (citation no. 30 on the IDS of 07/31/2006).

Ruano et al teaches a method for the analysis of haplotypes amplified from a single DNA molecule.

Regarding claim 1, Ruano et al teaches that a nucleic acid sample from a subject is diluted to form a solution containing a single copy of the target molecule (p.6297 – Dilutions; Fig 3), relevant to step (a). Relevant to step (b), the reference teaches the amplification of target DNA using two primer pairs (GR1, GR3 and GR2, GR4) that amplify a region comprising 3 polymorphic sites (i.e.: primers GR1 and GR3 type a TG deletion; primers GR2 and GR4 type two separate SNPs) (Fig 1; p.6297 – Target for amplification). Further relevant to step (b), the reference teaches that distant segments of an intact template molecule can be analyzed by PCR with multiple primer pairs for direct haplotype determination (p.6300 – Discussion). Relevant to step (c), Ruano et al teaches the genotyping of sites amplified from the single molecule dilution target DNA

by southern hybridization (Fig 4) and restriction digestion (Fig 3). Relevant to step (d), the reference teaches that information regarding the individual genotypes is combined to determine the haplotype of the subject (Fig 4; p.6298 – Typing and direct haplotype determination of SMP products).

Regarding claim 2, Ruano et al teaches that additional experiments are performed on sample DNA to resolve constituent haplotypes of heterozygous individuals (p.6298, right col., last paragraph; Fig. 3; Fig 4), and that each experiment followed the scheme present in Figure 3 of the reference, thus comprising steps (a)-(c) as recited in claim 1. The reference specifically teaches that for 'Person B' the experiment was repeated five times, and that four haplotypes (each comprising the component genotypes) were resolved (Fig 4; p.6299 – Individual B).

Regarding claims 4-6, Ruano et al teaches the analysis of a haplotype comprising polymorphic sites that are single nucleotide polymorphisms and a dinucleotide insertion/deletion (Fig 1).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ruano et al (1990) (citation no. 30 on the IDS of 07/31/2006).

Ruano et al teaches a method for the analysis of haplotypes amplified from a single DNA molecule.

Ruano et al teaches that a nucleic acid sample from a subject is diluted to form a solution containing a single copy of the target molecule (p.6297 – Dilutions; Fig 3), relevant to step (a) of claim 1. Relevant to step (b) of claim 1, the reference teaches the amplification of target DNA using two primer pairs (GR1, GR3 and GR2, GR4) that amplify a region comprising 3 polymorphic sites (i.e.: primers GR1 and GR3 type a TG deletion; primers GR2 and GR4 type two separate SNPs) (Fig 1; p.6297 – Target for amplification). Further relevant to step (b) of claim 1, the reference teaches that distant segments of an intact template molecule can be analyzed by PCR with multiple primer

pairs for direct haplotype determination (p.6300 – Discussion). Relevant to step (c) of claim 1, Ruano et al teaches the genotyping of sites amplified from the single molecule dilution target DNA by southern hybridization (Fig 4) and restriction digestion (Fig 3). Relevant to step (d) of claim 1, the reference teaches that information regarding the individual genotypes is combined to determine the haplotype of the subject (Fig 4; p.6298 – Typing and direct haplotype determination of SMP products). Relevant to claim 2, Ruano et al teaches that additional experiments are performed on sample DNA to resolve constituent haplotypes of heterozygous individuals (p.6298, right col., last paragraph; Fig. 3; Fig 4), and that each experiment followed the scheme present in Figure 3 of the reference, thus comprising steps (a)-(c) of claim 1. The reference specifically teaches that for 'Person B' the experiment was repeated five times, and that four haplotypes (each comprising the component genotypes) were resolved (Fig 4; p.6299 – Individual B). Thus Ruano et al teaches all of the limitations of claims 1 and 2, from which rejected claim 8 depends.

Ruano et al does not specifically teach the analysis of 12-18 genotype replicas.

Regarding claim 8, Ruano et al teaches repetition of experimentation to resolve genotypes (p.6298 – right col., last paragraph), and further teaches that errors in haplotype determination should be held in check by analyzing replicate vials (p.6300, left col., lns.43-45).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the haplotype determination methods of Ruano et al to produce and analyze 12-18 replicas. One would have been motivated to

create multiple genotype replicas based on the assertion of Ruano et al that such methods increase the accuracy of the analysis (p.6298 – right col., last paragraph; p.6300, left col., lns.43-45). One of skill in the art would recognize that creating an increased number of replica genotypes would lead to further increased accuracy of haplotype determination, and the skilled artisan would be capable of creating, for example, 12 genotype analyses of single-molecule dilutions (e.g. Ruano et al teaches twelve total analyses in Fig 4).

11. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ruano et al (1990) (citation no. 30 on the IDS of 07/31/2006) in view of Ross et al (citation no. 27 on the IDS of 07/31/2006).

The teachings of Ruano et al in are applied to claim 7 as they were previously applied to claim 8.

Ruano et does not teach the analysis of amplified polymorphic genotype markers using primer extension and mass spectrometric detection.

Ross et al teaches methods of multiplex genotyping using primer extension and mass spectrometry (p.1347, right col., lns.3-11). The reference teaches a method comprising the steps of amplification of 12 polymorphic loci and subsequent primer extension using oligonucleotide primers and ddNTPS (p.1350 – Experimental protocol, PCR). The reference further teaches analysis of the primer extension products by MALDI-TOF mass spectrometry (p.1350 – Experimental protocol, MS; Fig.2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the haplotype analysis methods of Ruano et al so as to have incorporated the primer extension/mass spectrometry based genotype detection methods of Ross et al. One would have been motivated to use the methods of Ross et al based on the teachings of Ross et al that primer extension/mass spectrometry based methods eliminate excess handling and can resolve many possible genotypes/loci using a single non-fluorescent primer (p.1347, left col., ln.37).

12. Claims 3 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruano et al (1990) (citation no. 30 on the IDS of 07/31/2006) in view of Drysdale et al (2000) (citation no. 9 on the IDS of 07/31/2006).

The teachings of Ruano et al are applied to claims 3 and 9-11 as they were previously applied to claim 8.

Ruano et al teaches a method for the determination of haplotypes amplified from a single DNA molecule and methods to obtain at least four genotype replicas, thus teaching all of the limitations of claims 1 and 2 (from which rejected claim 3 depends), as well as steps (a)-(d) of claim 9, and the limitations of claim 10.

Regarding the limitations of claim 11, Ruano et al teaches repetition of experimentation to resolve genotypes (p.6298 – right col., last paragraph), and further teaches that errors in haplotype determination should be held in check by analyzing replicate vials (p.6300, left col., lns.43-45).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the haplotype determination methods of Ruano et al to produce and analyze 12-18 replicas. One would have been motivated to create multiple genotype replicas based on the assertion of Ruano et al that such methods increase the accuracy of the analysis (p.6298 – right col., last paragraph; p.6300, left col., lns.43-45). One of skill in the art would recognize that creating an increased number of replica genotypes would lead to further increased accuracy of haplotype determination, and the skilled artisan would be capable of creating, for example, 12 genotype analyses of single-molecule dilutions (e.g. Ruano et al teaches twelve such analyses in Fig 4).

Ruano et al does not teach the comparison of a deduced haplotype with a haplotype from a control or a database of haplotypes from controls to determine association of the haplotype with a biological trait (as required by claim 3), or comparison of a deduced haplotype with known disease-associated haplotypes to indicate that the subject has, or is susceptible for, a disease (as required by step (e) of claim 9).

Drysdale et al teaches the use of β_2-adrenergic (β_2AR) receptor haplotypes in the prediction of response to albuterol (p.10486, left col., lns.6-8), which is a biological trait.

Regarding claim 3 and step (e) of claim 9, Drysdale et al teaches a collection of (β_2AR) haplotype pairs found in a cohort of asthmatics (p.10486, right col., lns.3-10; Table 2) (thus a database of haplotypes), as well as the association of the five most common haplotype pairs with patient response to albuterol (Fig.3; p.10487, left col.,

lns.1-25). The reference further teaches comparing a haplotype to the database of haplotypes and association data to determine association of the haplotype with a biological trait (Fig.3; p.10487, left col., lns.25-30).

It would have been prima facie obvious to one of skill in the art at the time the invention was made to have compared haplotypes determined by the methods of Ruano et al to a database of haplotypes as taught by Drysdale et al. One would have been motivated to perform a comparison of a haplotype determined by the methods of Ruano et al with a haplotype from a control, or with known disease-associated haplotypes, based on the assertion of Drysdale et al that haplotypes are more predictive of phenotype, and that individual SNPs may have poor predictive power as pharmacogenetic loci (p.10488, right col., lns.13-17). With specific regard to claim 11, it would have been obvious to create and analyze numerous replicas in a comparison of a haplotype determined for a subject with known disease-associated haplotypes, including producing 12-18 replicas, to increase the accuracy of the analysis, as discussed earlier in this rejection.

13. Claims 12-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruano et al (1990) (citation no. 30 on the IDS of 07/31/2006) in view of Rein et al (1998) (citation no.26 on the IDS of 07/31/2006).

The teachings of Ruano et al are applied to claims 12-18 as they were previously applied to claim 8.

Ruano et al teaches a method for the determination of haplotypes amplified from a single DNA molecule and methods to obtain at least four genotype replicas, thus teaching the limitations of steps (b)-(e) of claim 12 and claim 13. Ruano et al teaches the limitations of steps (b)-(e) of claim 17 (with regard to step (c) of claim 17, the teachings of Ruano et al with amplification of the diluted nucleic acid sample is discussed above, and the reference also teaches amplification of an undiluted nucleic acid sample (e.g. Fig 2) as required by step (c) of claim 17) and methods to obtain at least four genotype replicas, as required by claim 18.

Regarding the limitations of claim 14 (requiring that 12-18 genotype replicas are produced), Ruano et al teaches repetition of experimentation to resolve genotypes (p.6298 – right col., last paragraph), and further teaches that errors in haplotype determination should be held in check by analyzing replicate vials (p.6300, left col., lns.43-45); although Ruano et al does not specifically teach producing 12-18 replica genotypes by repetition of the diluting, amplifying, genotyping steps.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the haplotype determination methods of Ruano et al to produce and analyze 12-18 replicas, as required by claim 14. One would have been motivated to create multiple genotype replicas based on the assertion of Ruano et al that such methods increase the accuracy of the analysis (p.6298 – right col., last paragraph; p.6300, left col., lns.43-45). One of skill in the art would recognize that creating an increased number of replica genotypes would lead to further increased accuracy of haplotype determination, and the skilled artisan would be capable of

creating, for example, 12 genotype analyses of single-molecule dilutions (e.g. Ruano et al teaches twelve such analyses in Fig 4).

Ruano et al does not teach methods of comprising treating a sample with a composition that differentially affects an epigenetically modified nucleotide (step (a) of claim 12), or using bisulfite (claim 16) to modify a methylated nucleotide (claim 15), or digesting a nucleic acid sample with a methylation-sensitive restriction enzyme (step (a) of claim 17).

Rein et al teaches method for the identification of 5-metyhlcytosine and related modifications in DNA genomes (Table 1; p.2255, right col., first full paragraph).

Regarding claim 12, Rein et al teaches methods for analysis of 5-methylcytosine (m^5C, which is a modified nucleotide) by treating genomic DNA with a composition that differentially affects epigentically modified nucleotides by converting non-methylated C to U, and not altering m^5C (p.2258 – Differential base modification by bisulfite), relevant to step (a) of claim 12. Rein et al thus teaches effectively creating polymorphisms (the content at a given nucleotide position can be a C if the position is methylated, or U (which behaves similar to a T in subsequent base pairing processes) if the position is nonmethylated) based on the epigenetic methylation modification (Fig 2).

Regarding claim 15, Rein et al teaches the analysis of 5-methylcytosine (m^5C), which is a methylated nucleotide (p.2258 – Differential base modification by bisulfite).

Regarding claim 16, Rein et al teaches the use of bisulfite for the treatment of a nucleic acid sample (p.2258 – Differential base modification by bisulfite; Table 1; p.2255, right col., ln.25).

Regarding claim 17, Rein et al teaches methods for analysis of methylated bases at specific DNA sites use modification-sensitive restriction endonucleases (Table 1; p.2257 - Modification-sensitive restriction endonucleases (MSREs); Fig 1). Relevant to step (a) of claim 17, the reference teaches the digestion of a sample with restriction enzymes that are sensitive to base modification (i.e. will not digest methylated sites) and restriction enzymes that require base modification (i.e. will only digest methylated sites) (p.2257, left col., lns.14-24; Fig 1). Relevant to step (e) of claim 17, Rein et al teaches the analysis of the methylation dependent digestion of a sample by Southern analysis and PCR amplification (Fig 1; p.2258, left col., lns.15).

It would have been prima facie obvious to one of skill in the art at the time the invention was made to have modified the haplotype determination methods of Ruano et al so as to have included the methylation analysis methods of Rein et al. One would have been motivated to do so because Rein et al teaches that the status of methylation of any particular cytosine (i.e. 5-methylcytosine) in the genomes of eukaryotic cells plays a role in a variety of processes (p.2255, left col., first paragraph of introduction). One would have been motivated to use the bisulfite treatment of Rein et al (relevant to claims 12-16) because Rein et al teaches that such methods are highly sensitive, are amenable to rapid genomic sequencing, and provide positive display of m^5C (Table 1). One would have been motivated to use the MSRE method of Rein et al (relevant to claim 17 and 18) because Rein et al teaches that such methods provide a rapid analysis of large DNA regions, and are highly sensitive. With particular regard to step (e) of claim 17, the combination of the restriction enzyme digestion methods of Rein et al (as

summarized in Fig 1 of Rein et al) and the haplotype determination methods of Ruano et al would create a method where, for example, the DNA sample amplified by GR1, GR2, GR3, and GR4 (as from the nomenclature of Ruano et al) would be produce by restriction digestion (as taught in Fig 1 of Rein et al) instead of by a first PCR amplification with GR5 and GR6 (as taught by Fig 1 of Ruano et al). Thus the determined haplotype would include polymorphic markers such as SNPs (determined by PCR as taught by Ruano et al) that are next to (e.g. the polymorphic sites would be adjacent to the cut site determined by the action of an m^5C-requiring restriction enzyme) the methylation site analyzed by the restriction enzyme.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-6, 9, 12 and 15-17 of U.S. Patent Application No. 10/759,519. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the conflicting application recite methods for determining a haplotype of a subject by diluting a sample into a single molecule dilution, amplifying polymorphic sites in the diluted nucleic acid, determining the genotype of the polymorphic sites in the single molecule dilution, determining and a haplotype from the genotypes. The claims of the conflicting application further encompass obtaining replica genotypes, using primer extension and mass spectrometry, comparing determined haplotypes to haplotypes of control subjects and to databases of disease associated haplotypes, as well as the analysis of nucleic acids using bisulfite to modify methylated cytosine and methylation specific restriction enzymes. As such the claims of the conflicting application encompass all of the limitations of the claims of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

16. No claim is allowable. No claim is free of the prior art.

17. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Furlong et al (1993) teaches the analysis of flow-sorted single sperm cells, which contain a single molecule dilution of each human chromosome,

comprising amplification of nucleic acid regions comprising polymorphic sites to determine the haplotype of the chromosome contained in a flow-sorted single sperm cell.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days.

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Stephen Kapushoc
Art Unit 1634

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER